REMARKS

Claims 1-72 are pending. Claims 1, 4-7, 11, 15-22, 25, 28-32, 40, 42, 52 and 71 are amended. Claims 2-3, 8-10, 12-14, 23-24, 33-39, 41, 45-51, 53-70, and 72 remain unchanged. Claims 26-27 and 43-44 are canceled.

Claims 1-11, 15, 24-26, 28-32, 40-43, 45-50, 71 and 72 are rejected. Claims 12-14, 16-23, 27, 33-39, 44, and 51-70 are objected to as being dependent upon a rejected base claim.

THE AMENDMENT

Claim 1 has been amended to recite that the formulation is administered systemically, support for which may be found, for example, at page 5, lines 11-12 of the Specification. Claim 1 has been amended to recite that the formulation is administered less than 3.5 hours prior to anticipated sexual activity, support for which may be found, for example, on page 6, lines 17-19; page 9, lines 14-26, and page 24, lines 22-24 of the Specification. Support for "anticipated sexual activity" can be found, for example, at page 5, lines 6-8 of the Specification. Claim 1 has also been amended to recite that the formulation is rapid-release, support for which may be found, for example, at page 18, line 4 of the Specification. Claim 1 has been amended to recite that a systemically effective level of the active agent is achieved within 3.5 hours of administration, support for which may found, for example, at page 18, lines 4-8 of the Specification. Support for the aforementioned language can also be found in the parent application, U.S. Patent Application Serial No. 09/721,412, the disclosure of which was incorporated by reference at page 1, lines 7-9 of the Specification.

Claims 40 and 71 have been amended to recite systemically effective levels within 3.5 hours of administration, and claim 71 has been amended to recite a "rapid-release" formulation.

Claim 40 has been amended to recite drug administration effective to delay the onset of ejaculation during sexual activity, support for which can be found, for example, at page 5, lines 27-28 of the Specification.

Claims 25 and 42 have been amended to delete the term "clomipramine," which has necessitated the cancellation of Claims 26-27 and 43-44.

Claims 4-5, 11, 15-22, 28-32, and 52 have been amended to correct informalities such as typographical errors, corrections to claim dependencies and to recite consistent language.

Neither the cancellation of claims nor the amendment of pending claims should be construed as abandonment of any canceled subject matter.

No new matter has been added.

OBJECTION UNDER 37 C.F.R. §1.75(c)

Claim 8 has been objected to under 37 C.F.R. §1.75(c) as being of improper dependent form for failing to further limit the subject matter of a previous claim. In particular, the Examiner asserts that Claim 8 fails to further limit the prior claims since treatment is directed to premature ejaculation during sexual intercourse. The Examiner argues that no other sexual activity is disclosed or suggested. While the Examiner is correct that sexual intercourse is the only sexual activity specifically stated in the specification, that was merely listed as an exemplary sexual activity and the invention is not limited to such.

Applicants assert that one skilled in the art, e.g., a physician treating patients suffering from a sexual dysfunction, would understand that the term "sexual activity" encompasses numerous activities other than sexual intercourse. For example, masturbation would be one such activity that is also clearly understood to be a "sexual activity". More importantly, premature ejaculation, to which the instant invention is addressed, may well be of concern to participants of that activity.

Finally, the term "sexual activity" as used in the patent literature also has a breadth of meaning. See for example, U.S. Patent No. 6,455,564 to Meglasson et al., where the term "sexual activity" is recited in claims directed at treating male erectile disorder. The term is noted in the specification to include "sexual intercourse with or without orgasm, ejaculation, masturbation and sexual foreplay".

In conclusion, Applicants are entitled to the broadest interpretation of the claim language which this specification will support. The specification clearly intended to include other activities within the meaning of the term "sexual activity" because the specification recites that "The terms "treating" and "treatment" as used herein refer to the ability to increase an individual's ejaculatory latency (i.e., delay ejaculation) during sexual activity, particularly sexual intercourse,..." [emphasis added]. This, in combination with other patent language and the

knowledge of those skilled in the art, indicates that Claim 8 is proper. Applicants respectfully request withdrawal of the rejection.

REJECTION UNDER 35 U.S.C. §102(b) OVER ROWLAND

Claims 1-11, 24-26 and 40-43 stand rejected under 35 U.S.C. §102(b) as being anticipated by Rowland et al. (1998) *Drugs of Today* 34(10):879-899 (hereinafter "Rowland").

Rowland is cited as disclosing the treatment of premature ejaculation by administration of clomipramine, administered less than one hour prior to ejaculation (Results/effectiveness heading for all clomipramine studies). The Examiner notes that administration may occur at much as 4-6 hours prior (page 892, lines 1-2). The Examiner also notes that while Rowland does not describe a rapid-release dosage, no mention is made of sustained or extended release that would teach away from the instant invention.

Claim 1, as amended recites a method for treating premature ejaculation by "systemically" administering a "rapid-release" pharmaceutical formulation containing an antidepressant "less than 3.5 hours prior to anticipated sexual activity", wherein the formulation releases the drug at a rate that provides a "systemically effective level of the drug within 3.5 hours of administration." Claim 40, as amended, recites a pharmaceutical formulation for treating premature ejaculation, comprising a rapid-release formulation of an antidepressant drug "in an amount effective to delay the onset of ejaculation by the individual during sexual activity" and provides a "systemically effective level of the drug within 3.5 hours of administration."

The Examiner has interpreted the reference as disclosing administration of clomipramine less than an hour prior to ejaculation, citing the table on pages 890-891. Applicants respectfully disagree with the Examiner's interpretation of the reference, for the following reasons. Rowland et al., on page 889, second column, under the heading "1) Tricyclic antidepressants (Table I)," discloses administration of clomipramine in three different ways:

(1) chronically, at 25 mg/day or 50 mg/day;

(2) on an as-needed basis 12-24 hours prior to anticipated intercourse; and

(3) on an as-needed basis 4-6 hours prior to intercourse.

There is no teaching or suggestion of administering clomipramine less than 3.5 hours prior to anticipated sexual activity (Claim 1) or in an amount effective to delay the onset of

ejaculation by the individual during sexual activity (Claim 40). With respect to the entries in Table I pertaining to clomipramine, the data in the right-hand column (entitled "Results/effectiveness") pertains to "ejaculatory latency," which the authors define in the conventional sense to mean the time period between vaginal intromission and ejaculation (see page 881 of the reference, under "Latency to ejaculation"). Ejaculatory latency does not refer to the time period between drug administration and ejaculation. See, for example, the data on page 890 relating to a study by Althof et al. In that study, as may be seen under the column "Dose/frequency," clomipramine was given 25 mg/day or 50 mg/day, on an ongoing (chronic) basis. The table indicates, in the right-hand column, that those patients receiving 25 mg/day experienced an increase in ejaculatory latency from a baseline of 81 seconds to 202 seconds, while patients receiving 50 mg/day experienced an increase in ejaculatory latency from a baseline of 81 seconds to 419 seconds. There is no indication, in the table, that clomipramine was ever administered less than 4 hours prior to sexual activity. Any references in the Rowland table to administration of drugs at 30 minutes or 1 hour before coitus, refer to lidocaine/prolacaine and S-S cream, respectively, cream formulations of drugs that are unrelated to the methods and formulations presently claimed.

As noted above, the Examiner indicates that while Rowland does not describe a rapid-release dosage, no mention is made of sustained or extended release that would teach away from the instant invention. However, anticipation of a claimed invention by a prior art reference under 35 U.S.C. §102(b) requires the presence in a single prior art reference of each and every element of a claimed invention. The "rapid-release" aspect of the claimed invention is related to the recitation of administration less than 3.5 hours prior to anticipated sexual activity, as well as the formulation providing a systemically effective level of the drug within 3.5 hours of administration. Rowland does not teach or even suggest a rapid-release formulation and does not teach a dosing regimen that would suggest the desirability of a rapid-release formulation. There mere fact that Rowland does not teach away from a rapid-release formulation does not constitute anticipation.

Applicants' claimed method and formulation relate to an as-needed basis administration, with "as-needed basis" defined in the specification to mean that the method does not involve chronic pharmacotherapy. Rather, administration is on an as-needed basis, which involves

administration shortly before anticipated sexual activity (page 5, lines 6-8 of the specification). This typically includes administration immediately prior to sexual activity (page 9, line 21); up to about 2 or 3 hours prior to anticipated sexual activity (page 6, lines 17-19); about 0.25 to 3.5 hours, about 0.5 to 3 hours, or about 1 to 2.5 hours prior to anticipated sexual activity (page 9, lines 21-23); or within a 0.25 to 3-hour window prior to anticipated sexual activity (page 24, lines 23-24). Claim 1 has been amended to includes these ranges in the recitation of "less than 3.5 hours."

Accordingly, Applicants are not acquiescing in the rejection but have nevertheless amended Claims 1 and 40 to clarify the recited method and formulation relative to the disclosure of Rowland. Claim 1 now specifies that that the formulation is administered less than 3.5 hours prior to engaging in sexual activity, and Claims 1 and 40 have both been amended to recite that the formulation is rapid-release and that the drug is released to provide a systemically effective level of drug within 3.5 hours of administration. Since the absolute minimum time period disclosed by Rowland is 4 hours prior to sexual activity, with "as needed" administration actually defined as 12-24 hours prior to sexual activity (see page 889, right-hand column), the presently amended claims 1 and 40 are clearly distinguished over the reference.

Accordingly, since Rowland does not teach, or even suggest the invention as presently claimed, Applicants assert that the invention is patentable under 35 U.S.C. §102(b).

REJECTION UNDER 35 U.S.C. §102(b) OVER SMITH

Claims 1-11, 15, 24-26, 28-32, 40-43 and 45-50 stand rejected under 35 U.S.C. §102(b) as being anticipated by U.S. Patent No. 5,922,341 to Smith et al. (hereinafter "Smith").

Smith is cited as disclosing a method for delaying the onset of ejaculation through the use of various compounds (Abstract), including antidepressants (col. 3, lines 20-25) such as clomipramine (col. 5, line 12). The Examiner also notes that while Smith does not describe a rapid-release dosage, no mention is made of sustained or extended release that would teach away from the instant invention.

As noted above, Claim 1, as amended recites a method for treating premature ejaculation by systemically administering a rapid-release formulation less than 3.5 hours prior to anticipated sexual activity, and the formulation releases drug at a rate that provides systemically effective

levels of drug within 3.5 hours of administration. Claim 40, as amended, recites a pharmaceutical formulation for treating premature ejaculation, comprising a rapid-release formulation in an amount effective to delay the onset of ejaculation during sexual activity and that releases drug at a rate effective to provide systemically effective levels of drug within 3.5 hours of administration.

Therefore, the invention as presently claimed relates to systemic administration. Systemic administration is to be contrasted with local administration, which is the primary focus of the Smith reference. Local administration would not be expected to provide "systemically effective" levels of an active agent as is required by Applicants' claimed invention. Also, although Smith states that "with some active agents, [administration can be] just prior to intercourse" (column 12, lines 7-8), Smith does not teach or suggest drug administration less than 3.5 hours prior to sexual activity and/or systemic levels achieved within 3.5 hours of administration, as is required by the amended claims.

In addition, contrary to the Examiner's assertion, Smith does not explicitly describe oral or transmucosal administration of an active agent. Col. 9, lines 39-56 of Smith describes transurethral delivery as well as other types of local delivery and mentions intracavernosal injection, topical application and transdermal application. This section of Smith also mentions that "depending on the intended mode of administration, the pharmaceutical compositions may be in the form of solid, semi-solid or liquid dosage forms, such as, for example, tablets, suppositories, pills, capsules, powders, liquids, suspensions, creams, ointments, lotions or the like, preferably in unit dosage form suitable for single administration of a precise dosage". Although various dosage forms are described in this section of the Smith specification, it is made clear throughout the Smith patent that drug administration is intended to be local, and that such local delivery contrasts with oral, systemic administration. See the discussion in the Background section of Smith, regarding the distinctions between oral, systemic delivery and local administration, that latter being the focus of the Smith invention. Also see col. 12, lines 16-19, where Smith states that "[b]y administering the drug locally, the side effects, drug interactions and disease considerations of systemic (e.g., oral) drug administration are avoided." Applicants assert that this statement evidences that Smith actually teaches away from systemic methods and compositions, as are presently claimed.

Finally, as noted above, the Examiner indicates that while Smith does not describe a rapid-release dosage, no mention is made of sustained or extended release that would teach away from the instant invention. As Applicants argued above with regard to the Rowland reference, anticipation requires the presence in a single prior art reference of each and every element of a claimed invention. Smith does not teach or even suggest a rapid-release formulation and does not teach a dosing regimen that would suggest the desirability of a rapid-release formulation. There mere fact that Smith does not teach away from a rapid-release formulation does not constitute anticipation.

Accordingly, since the Smith reference does not teach, or even suggest the invention as presently claimed, Applicants assert that the invention is patentable under 35 U.S.C. §102(b).

REJECTION UNDER 35 U.S.C. §103(a), OVER ROWLAND OR SMITH

Claims 71-72 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Rowland or Smith.

Rowland is cited as disclosing the treatment of premature ejaculation by administration of clomipramine, administered less than one hour prior to ejaculation. Smith is cited as disclosing a method for delaying the onset of ejaculation through the use of various compounds, including antidepressants such as clomipramine. The Examiner also notes that while neither Rowland or Smith describe a rapid-release dosage, no mention is made of sustained or extended release that would teach away from the instant invention. The Examiner also notes that neither reference mentions packaging the composition in a kit, but relies on the knowledge in the art that pharmaceuticals are routinely packaged in kits.

Claim 71, as amended, recites a packaged kit for a patient to use in the treatment of premature ejaculation, comprising a rapid-release pharmaceutical formulation that releases the drug at a rate effective to provide a systemically effective level of the drug within 3.5 hours of administration to a patient.

For the reasons set forth above, Rowland and Smith do not teach or suggest a ***rapid-release*** formulation that provides ***systemic*** delivery within 3.5 hours of administration to a patient. Therefore, even assuming for arguments sake that pharmaceuticals are routinely packaged in kits, one of skill in the art would still not arrive at Applicants' claimed invention

after reviewing the Rowland or the Smith reference since they do not teach or suggest the rapid-release and systemic features of the claimed invention.

OTHER REFERENCES NOTED

Girgis et al. (1982) *Andrologia* 14(4):364-368 and Assalian (1988) *The Journal of Sex Research* 24:213-215 are cited for their equivalent teaching of the use of clomipramine in the treatment of premature ejaculation. However, they do not form the basis of a rejection under 35 U.S.C. §102 or §103.

Applicants have reviewed these references and agree with the Examiner's implicit finding that the references do not disclose or suggest, either individually or in combination, the presently claimed invention.

SUMMARY

The above arguments and amendments to the Claims are submitted for the purpose of facilitating allowance of the Claims and a sincere effort has been made to place this application in condition for allowance. An early notice of allowance is earnestly requested.

If in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned at (650) 330-4916.

Respectfully submitted,

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